

The maternal and neonatal outcomes of pregnant women with definite COVID-19

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Abstract

Background: This study aimed to assess the symptoms and clinical laboratory data of pregnant women with COVID-19 in their second or third trimester of pregnancy as well as their maternal and neonatal outcomes.

Methods: This retrospective observational study was conducted on 177 pregnant women with COVID-19 who were admitted to Yas hospital (affiliated with Tehran University of Medical Sciences), and Ali-ibn-Abi-Talib hospital (affiliated with Zahedan University of Medical Sciences).

Results: There was significant higher complaints including fever (p-value=0.015), cough (p-value=0.028), fatigue (p-value=0.002), dyspnea (p-value=0.022), and lower hemoglobin level (p-value=0.009) in patients who were in their third trimester compared to those who were in their second trimester. 9.6% (n=17) of the patients had severe disease and needed ICU admission. There was a significant variation regarding gestational age (p-value=0.022) in pregnant women admitted to ICU compared to the other ones. During the study, delivery happened in 108 (61%) pregnant women. Fetal distress following meconium deification (p-value=0.041), need to MGSO4 (p-value=0.001), IUFD (p-value=0.006), need for blood transfusion (p-value=0.004), and neonatal death (p-value<0.001) were significantly higher in patients who needed ICU admission.

Conclusion: Higher gestational weeks are the main risk factor for severe COVID-19 disease. Although vertical transmission is rare; due to the higher risk of perinatal outcomes, the delivery should be done in a center with a NICU department.

Key Words: COVID-19, Gestational age, Morbidity, Mortality, Pregnancy, Pregnancy trimesters.

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1- INTRODUCTION

Coronavirus disease 2019 (COVID-19) has adversely affected several aspects of healthcare worldwide (1-3). COVID-19 is characterized by a diverse collection of symptoms in individuals with varying severity, from an asymptomatic presentation and mild symptoms to respiratory failure, multi-organ dysfunction, and death (4-8).

Since the official recognition of SARS-CoV-2 by the World Health Organization (WHO) on February 2020, and the subsequent global dissemination of the virus, efforts have been directed towards developing a thorough finding out of the pathophysiology of the disease, identification of possible risk factors, and markers of poor prognosis in addition to the search for effective treatment regimens (9). Among the individuals who are more likely to be vulnerable to the infection, pregnant women are of particular interest.

Pregnancy is characterized by a number of adaptations to the growing fetus, including physiological and pathophysiological changes in the respiratory system, immune system, and several other organ systems, which may inadvertently result in higher susceptibility to respiratory infections. For instance, there is a decreased number of CD4+ and CD8+ lymphocytes, a shift of CD4+ immune phenotype from a Th1 to Th2 profile that promotes humoral response over cellular immune response, hypercoagulability, and decreased respiratory volumes during the pregnancy (10, 11).

Indeed, several complications such as higher mortality rate and preterm birth have been previously reported in pregnant women affected by influenza virus, hepatitis E virus, malaria, and other coronavirus-related diseases, including severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) (12). These changes may also

result in adverse outcomes of SARS-CoV-2 infection in pregnancy (13), despite initial studies suggesting a similar risk of developing severe disease (14).

While the clinical manifestation of COVID-19 in pregnancy and its adverse outcomes have been evaluated in a few studies, the full spectrum of its symptoms in the full span of pregnancy, and the maternal and fetal outcomes have not been thoroughly assessed. This retrospective observational study compares the incidence of symptoms and clinical laboratory data of women with COVID-19 in their second and third trimester of pregnancy as well as maternal and neonatal outcomes of the admitted patients in intensive care units and non-intensive care settings.

2- METHODOLOGY

This retrospective observational study examined the characteristics of 177 pregnant women with definite COVID-19 who referred to the prenatal clinics of Yas hospital (affiliated with Tehran University of Medical Sciences) (147 pregnant women), and Ali-ibn-Abi-Talib hospital (affiliated with Zahedan University of Medical Sciences) (30 pregnant women), from February to September 2021.

The census sampling method was applied. Singleton pregnant women aged more than 18 years with positive real-time reverse transcription PCR (RT-PCR) test or COVID-19 features in lung CT-scan were included in this study. Patients who withdrew to participate at any time during the study were excluded from the study.

Nasopharyngeal swab specimen was evaluated by kit (Modular DxKit, Wuhan CoV E & RdRP genes) and conventional RT-PCR (for the N region using N1F and N3R primers) with sensitivity of 95% (15).

The patient hospital's medical records, including medical information, the initial vital sign, complete blood count (CBC),

blood group, creatinine, blood urea nitrogen, international normalized ratio, alanine aminotransferase, aspartate aminotransferase, procalcitonin, albumin, lactate dehydrogenase, prothrombin time, D-dimer, C-reactive protein, erythrocyte sedimentation rate, and a lung CT-scan (in some cases) were used for data gathering.

Furthermore, neonatal outcomes including ICU Admission, neonatal respiratory distress syndrome (RDS), pneumonia, need for continuous positive airway pressure (CPAP), endotracheal intubation, phototherapy, blood transfusion, and death were collected.

2-2. Statistical Analysis

All the data were analyzed using SPSS version 24.0. P-value < 0.05 was considered as the level of statistical significance. Independent T-test and Non-

parametric Mann–Whitney U-test were performed to evaluate the quantitative data and Chi-square and Fisher's exact test to assess the qualitative data.

3- RESULTS

The mean age of participants was 32.11 ± 6.07 with a range of 18 to 48 years. Most of the cases (89.3%) were in the third trimester of their pregnancy, and only 10.7% were in their second trimester. The participants' gestational age ranged from 12 to 40 weeks. The average BMI was 26.37 ± 3.29 kg/m².

Hypothyroidism was the most common (17.5%) underlying disease followed by gestational diabetes in 29 (16.6%) women. Furthermore, 65 (36.5%) of pregnant women had a history of influenza vaccination. The baseline information is summarized in **Table 1**.

Table-1: The baseline information

Characteristics (N=177)		
Age (years)		32.14±6.07
Gestational age (weeks)		33.61±6.09
Gravid		2.37±1.38
Parity		1.07±1.1
Abortion		0.46±0.81
Body mass index (kg/m ²)		26.37±3.29
Positive past medical history		79 (44.3)
Habit history	Smoking	3 (2.9)
	Alcohol	2 (1.9)
	Hookah	1 (0.9)
	Methadone	1 (0.9)
Blood group	A	47 (27.6)
	B	44 (25.9)
	AB	13 (7.3)
	O	66 (38.8)
Positive RH antigen		159 (93.5)

The definite diagnosis of COVID-19 was done with positive PCR tests in 158 (88.8%) women, abnormal lung CT-scan in 19 (10.7%) and both in one woman. The average time from symptom onset to refer

to hospital was 4.99 ± 3.16 days. The mean oxygen saturation was 95.12 ± 3.9 at the time of the patients' arrival to the emergency department of our hospitals.

The COVID-19 symptoms varied among the patients; cough and fever were the most common complaints. Furthermore, there was significant higher complaints including fever (p-value=0.015), cough (p-value=0.028), fatigue (p-value=0.002), and

dyspnea (p-value=0.022), as well as lower hemoglobin level (p-value=0.009) in patients who were in their third trimester compared to those who were in their second trimester (**Table 2**).

Table-2: COVID-19 symptoms and lab test findings according to the patients' trimester

Symptom/Lab test	N (%) or Mean±SD			P-value
	Total (N=177)	Trimester two (N=19)	Trimester three (N=158)	
Asymptomatic	39 (21.9)	0	39 (24.7)	0.008
Fever	83 (46.6)	14 (73.7)	69 (43.7)	0.015
Chill	23 (12.9)	5 (26.3)	18 (11.4)	0.078
Sore throat	27 (15.2)	4 (21.1)	23 (14.6)	0.498
Appetite loss	3 (1.7)	0	3 (1.9)	1.000
Headache	19 (10.7)	3 (15.8)	16 (10.1)	0.435
Cough	86 (48.3)	14 (73.7)	72 (45.6)	0.028
Nausea	15 (8.4)	3 (15.8)	12 (7.6)	0.207
Vomiting	12 (6.7)	1 (5.3)	10 (6.3)	1.000
Fatigue	21 (11.8)	7 (36.8)	13 (8.2)	0.002
Myalgia	39 (21.9)	7 (36.8)	31 (19.6)	0.134
Dyspnea	66 (37.1)	12 (63.2)	54 (34.2)	0.022
Smell loss	6 (3.4)	1 (5.3)	5 (3.2)	0.499
Taste loss	2 (1.1)	0	2 (1.3)	1.000
WBC (*10 ³)	9.22±3.99	7.61±5.3	9.45±3.77	0.058
Hemoglobin (g/dL)	11.91±1.59	11.01±1.34	12.01±1.58	0.009
Platelet (*10 ³)	189.29±78.55	193.73±83.83	188.56±78.37	0.788
Creatinine (mg/dL)	0.81±0.56	0.73±0.11	0.82±0.59	0.541
BUN (mg/dL)	14.45±6.98	14.77±6.12	14.42±7.12	0.840
PT (seconds)	13.38±4.82	12.53±0.51	13.45±5.03	0.587
INR	1.09±0.37	1.02±0.05	1.10±0.38	0.575
ALT (U/L)	36.77±39.34	45.5±33.67	35.62±40.15	0.321
AST (U/L)	41.86±45.58	50.44±36.45	40.83±46.82	0.404
PCT (ng/mL)	0.10±0.14	0.01±0	0.12±0.14	0.202
Albumin (g/dL)	3.37±0.51	3.2±0.14	3.38±0.52	0.629
LDH (IU/L)	513.02±265.31	488.43±243.07	517.52±269.59	0.683
D-dimer (ng/mL)	1024.98±1749.00	726.2±1218.95	1101.46±1848.18	0.455
CRP (mg/L)	37.78±40.98	30.2±31.16	38.96±42.57	0.334
ESR (mm/hr)	39.53±27.04	40.93±26.46	39.30±27.27	0.830

WBC: White blood cell, BUN: Blood urea nitrogen, PT: Prothrombin time, INR: International normalized ratio, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, PCT: Procalcitonin, LDH: Lactate dehydrogenase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate.

9.6% (17) of the pregnant women had severe disease and needed ICU admission. Maternal mortality was reported in 4.5% (8) of the participants. There was a

significant variation regarding gestational age (p -value=0.022) in pregnant women who were admitted in ICU in comparison to the other ones (**Table 3**).

Table-3: Comparison of the baseline information between non-ICU admission and ICU admission patients

Variables		non-ICU (N=160)	ICU (N=17)	P-value	
Maternal age (years)		32.06±5.89	32.52±7.78	0.590	
Gestational age (weeks)		34.06±5.74	30.94±5.73	0.022	
Body mass index (kg/m ²)		26.37±3.33	26.28±3.09	0.908	
Time from symptom onset to hospitalization (hours)		5.07±3.24	4.56±2.8	0.624	
Blood group	A	44 (28.4)	3 (20)	0.071	
	B	36 (23.2)	8 (53.3)		
	AB	13 (8.4)	0		
	O	62 (40)	4 (26.7)		
	RH positive		146 (94.2)	13 (86.7)	0.251
	Influenza vaccination		62 (38.7)	3 (17.6)	0.262

During the study, delivery happened in 108 (61%) pregnant women, among whom 93 had cesarean section delivery. On average, the Apgar minute one and five were 8.25 ± 1.73 and 9.57 ± 0.94 , respectively. The mean neonate weight was 3086.94 ± 741.04 grams with a range of 970 to 4900. About 52% of neonates were boys and 48% were girls.

For all newborns, the nasopharyngeal PCR was performed, among whom two neonates had positive results. In addition, for one neonate, the nasopharyngeal PCR was requested during the NICU hospitalization because of the suspected symptoms, which was positive. The mean hospitalization duration in newborns was 3.78 ± 3.27 days with a range of 1 to 18.

In comparison, delivery and neonatal outcomes between non-ICU admission and ICU admission patients, fetal distress following meconium deification (p -value=0.041), need to MGSO₄ (p -value=0.001), IUFD (p -value=0.006), need for blood transfusion (p -value=0.004), and neonatal death (p -value<0.001) were

significantly higher in patients who needed ICU admission (**Table 4**).

4- DISCUSSION

Not surprisingly, pregnant women are more susceptible to infections; physiological alteration including cardiopulmonary overload and immune system suppression are related causes. One study (15) indicated that the rate of hospitalization and severe COVID-19 diseases is more than five folds higher in pregnant women compared to the non-pregnant population, 31.5% vs. 5.8%, respectively.

Although fever, cough and lymphocytopenia are the most common findings in COVID-19 infected pregnant women, the COVID-19 presentation varied during the pregnancy and the significantly higher fatigue, dyspnea and above mentioned symptoms were reported in our patients who were in their third trimester progressing gestational weeks result in severe disease and ICU admission (16).

Table-4: Comparison of delivery and neonatal outcomes between non-ICU admission and ICU admission patients

Variables	non-ICU N=103	ICU N=5	P-value
Fetal distress following meconium deification	15 (14.5)	3 (60)	0.041
IUFD	1 (0.97)	2 (40)	0.006
Need to MGSO4	11 (10.6)	4 (80)	0.001
PROM	5 (4.8)	0	1.000
Postpartum hemorrhage	8 (7.7)	1 (20)	0.364
Breast feeding	48 (46.6)	0	0.048
NICU Admission	24 (23.3)	2 (40)	0.159
RDS	6 (5.8)	0	1.000
CPAP	7 (6.7)	1 (20)	0.164
Endotracheal intubation	4 (3.8)	1 (20)	0.144
Pneumonia	1 (0.97)	0	1.000
Phototherapy	9 (8.7)	0	1.000
Blood transfusion	6 (5.8)	3 (60)	0.004
Death	3 (2.9)	4 (80)	<0.001

IUFD: Intrauterine fetal demise, PROM: Premature rupture of membranes, RDS: Neonatal respiratory distress syndrome, CPAP: Continuous positive airway pressure.

Progressing gestational weeks are reported to result in severe disease and ICU admission (16), as it was also mentioned in our study regarding the patients who were in their third trimester. In addition to higher gestational weeks and third-trimester pregnancy, obesity, hypertension, diabetes mellitus, and maternal age greater than 40 years are the main risk factors for death, ICU admission and severe disease in pregnant women (17).

The well-known negative impacts of COVID-19 are preterm labor, preeclampsia and cesarean delivery (16). The most common indication for cesarean section was fetal distress (18). Conversely, cesarean section itself increases the risk of postpartum infection, hemorrhage, and thromboembolic complications that worsen the prognosis (19).

Similar to our findings, although the risk of vertical transmission is reported rare in former studies; perinatal outcomes including fetal distress, NICU admission,

and perinatal mortality are reported in mothers with COVID-19 especially mothers with severe diseases (16, 20).

Currently, our knowledge about the mechanism of COVID-19 during pregnancy, its impact on the pregnant women and her fetus, and the best approaches in management of the pregnant women is little. Hence, future studies seem to be required for filling this gap of science (21).

4-1. Limitations of the study

The study had some limitations including the retrospective nature of the study design, lack of non-pregnant and outpatient pregnant control group, and lack of the patients' trend of clinical and laboratory parameters. The strength of our study was its large sample size and multicentric setting of the study.

5- CONCLUSION

It seems that higher gestational weeks is a main risk factor for severe COVID-19

disease. Although the vertical transmission is rare, due to the higher risk of perinatal outcomes, the delivery should be done in a center with NICU department.

6- ETHICAL CONSIDERATION

This research was approved by the ethics committee of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1400.864). Written informed consents were taken from all participants.

7- ACKNOWLEDGEMENTS

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7- CONFLICT OF INTERESTS

None.

8- REFERENCES

1. Wang C-L. Impact of COVID-19 on Pregnancy. *International journal of medical sciences*. 2021; 18(3):763.
2. Shaukat N, Ali DM, Razzak J. Physical and mental health impacts of COVID-19 on healthcare workers: a scoping review. *International journal of emergency medicine*. 2020; 13(1):1-8.
3. Leite H, Lindsay C, Kumar M. COVID-19 outbreak: implications on healthcare operations. *The TQM Journal*. 2020.
4. Allen WE, Altae-Tran H, Briggs J, Jin X, McGee G, Shi A, Raghavan R, Kamariza M, Nova N, Pereta A, Danford C, Kamel A, Gothe P, Milam E, Aurambault J, Primke T, Li W, Inkenbrandt J, Huynh T, Chen E, Lee C, Croatto M, Bentley H, Lu W, Murray R, Travassos M, Coull BA, Openshaw J, Greene CS, Shalem O, King G, Probasco R, Cheng DR, Silbermann B, Zhang F, Lin X. Population-scale longitudinal mapping of COVID-19 symptoms, behaviour and testing. *Nature Human Behaviour*. 2020; 4(9):972-82.
5. Chan AT, Brownstein JS. Putting the Public Back in Public Health - Surveying Symptoms of Covid-19. *New England Journal of Medicine*. 2020; 383(7):e45.
6. Kim G-U, Kim M-J, Ra SH, Lee J, Bae S, Jung J, Kim SH. Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. *Clinical microbiology and infection*. 2020; 26(7):948. e1. e3.
7. Ye G, Pan Z, Pan Y, Deng Q, Chen L, Li J, Ye G, Pan Z, Pan Y, Deng Q, Chen L, Li J, Li Y, Wang X. Clinical characteristics of severe acute respiratory syndrome coronavirus 2 reactivation. *Journal of Infection*. 2020; 80(5):e14-e7.
8. Guan W-j, Ni Z-y, Hu Y, Liang W-h, Ou C-q, He J-x, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS, China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *New England Journal of Medicine*. 2020; 382(18):1708-20.
9. Wenling Y, Junchao Q, Xiao Z, Ouyang S. Pregnancy and COVID-19: management and challenges. *Revista do Instituto de Medicina Tropical de São Paulo*. 2020; 62.
10. Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. *N Engl J Med*. 2014; 370(23):2211-8.
11. Wastnedge EAN, Reynolds RM, van Boeckel SR, Stock SJ, Denison FC, Maybin JA, Critchley HOD. Pregnancy and COVID-19. *Physiological Reviews*. 2020; 101(1):303-18.
12. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, Vecchiet J, Nappi L, Scambia G, Berghella V, D'Antonio F. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM*. 2020; 2(2):100107.

13. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. *Cmaj.* 2021; 193(16):E540-E8.
14. Chen L, Li Q, Zheng D, Jiang H, Wei Y, Zou L, Feng L, Xiong G, Sun G, Wang H, Zhao Y, Qiao J. Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China. *New England Journal of Medicine.* 2020; 382(25):e100.
15. Yavarian J, Shafiei-Jandaghi NZ, Sadeghi K, Shatizadeh Malekshahi S, Salimi V, Nejati A, et al. First Cases of SARS-CoV-2 in Iran, 2020: Case Series Report. *Iran J Public Health* 2020; 49:1564-1568.
16. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, Vecchiet J, Nappi L, Scambia G, Berghella V, D'Antonio F. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM.* 2020 May; 2(2):100107.
17. Salvatori G, De Rose DU, Concato C, Alario D, Olivini N, Dotta A, Campana A, (2020) Managing COVID-19-positive maternal-infant dyads: an Italian experience. *Breastfeed Med* 15:347–348.
18. Markin L, Fartushok T, Mrochko Y, Pidhirnyj Y. MANAGEMENT OF PREGNANT WOMEN WITH COVID-19 - OWN EXPERIENCE. *Georgian Med News.* 2022 Feb; (323):38-47.
19. Liu S, Liston RM, Joseph KS, Heaman M, Sauve R, Kramer MS (2007) Maternal mortality and severe morbidity associated with low-risk planned cesarean delivery versus planned vaginal delivery at term. *CMAJ* 176:455–460.
20. Goh XL, Low YF, Ng CH, Amin Z, Ng YPM (2021) Incidence of SARS-CoV-2 vertical transmission: a meta-analysis. *Arch Dis Child Fetal Neonatal Ed England* 106:112–113.
21. Clemenza S, Zullino S, Vacca C, Simeone S, Serena C, Rambaldi MP, Ottanelli S, Vannuccini S, Bonizzoli M, Peris A, Micaglio M, Petraglia F, Mecacci F. Perinatal outcomes of pregnant women with severe COVID-19 requiring extracorporeal membrane oxygenation (ECMO): a case series and literature review. *Arch Gynecol Obstet.* 2022 May; 305(5):1135-1142.